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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,194	10/08/2001	Nathalie Elbaz	33339/208804	1669

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EXAMINER	
WAX, ROBERT A	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 11/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,194	ELBAZ ET AL.	
	Examiner	Art Unit	
	Robert A. Wax	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *6-8 and 15-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 9-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-20* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10092003* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, claims 1-5 and 9-14 in Paper No. 10092003 is acknowledged. The traversal is on the ground(s) that no lack of unity was held in the PCT and that reference AF121259, used to buttress the holding of lack of unity, was published after the priority date of 4 August 1998. This is not found persuasive. Lack of unity is revisited at each stage of an application including Chapter I, Chapter II and the National stage. No preceding determination is binding for a later stage. Also, the International Filing Date of 2 August 1999 is the earliest date accorded this application under 35 USC 371 and the publication date of AF121259, January 1999, precedes this date. Thus, the inventions of claims 1-20 do not involve only a single inventive concept as outlined in the restriction requirement.

The requirement is still deemed proper and is therefore made FINAL.

Information Disclosure Statement

2. The information disclosure statement filed February 5, 2001 has been considered. Please see the attached initialed PTO-1449.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2-4 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for fragments for the detection of SEQ ID Nos. 1, 3, 5, 7 or 9, does not reasonably provide enablement for homologous sequences thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

In *Ex parte Forman* (230 USPQ 546) (later upheld by the CAFC, see *In re Wands*, 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Circ. 1988)), the Board of Patent Appeals and Interferences considered the issue of enablement in molecular biology. The Board held that the following factors should be considered to determine whether the claimed invention would require of the skilled artisan undue experimentation:

1) Quantity of experimentation necessary;

2) Amount of direction or guidance presented;

3) Presence or absence of working examples;

4) Nature of the invention;

5) State of the prior art;

6) Relative skill of those in the art;

7) Predictability or unpredictability of the art;

8) Breadth of the claims.

The nature of this invention is the use of the fragments to detect the presence of specific sequences. It is unclear exactly what is meant by "homologous sequence" (see rejection for indefiniteness below) but if it is considered that a homologous sequence is

one that has a different sequence but the same function, it would require undue experimentation to determine which of such different sequences would, in fact, have the same function. The quantity of experimentation is immense. Each nucleotide of eh complement of each of SEQ ID Nos. 1, 3, 5, 7 or 9 would have to be changed and tested one by one. The length is not limited only to 400 base pairs since the claim recites, "comprising 20 to 400 bp". The amount of direction or guidance provided by the specification is essentially none, so the practitioner of this invention would not even have a starting place. This is not remedied by the lack of working examples in the specification. The state of the prior art is such that those of skill know how to detect nucleotide sequences but still requires knowledge of what sequences to use as the probes; the level of skill in this art is high. Notwithstanding, the majority of the so-called Forman factors argue toward a conclusion of nonenablement.

5. Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement because the specification, while being enabling for host cells cotransformed with two vectors encoding at least SEQ ID No. 5 and the C-terminal end of the AT2 receptor, respectively, does not reasonably provide enablement for host cells cotransformed with vectors encoding mutations of the recited protein fragments. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to produce the invention commensurate in scope with these claims. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the

invention. This claim contains the language, "mutated or not" and it would require undue experimentation on the part of the practitioner in the art to make all possible mutations.

The factors to be used to determine nonenablement are discussed above.

In order for one skilled in the art to produce mutated sequences, one would have to either mutate the known single sequence provided by applicant, by deletion, insertion or substitution of any number of the nucleotides. Therefore, the language of the claims encompasses an inordinate number of possible sequences. The specification does not provide direct guidance for any such mutations. Thus, this represents a large amount of experimentation. The level of skill in the art would have been such that the artisan could easily alter the codons in accordance with another preferred codon that encodes the same amino acid, without altering the primary structure of the protein, and therefore without altering the protein's activity. However, the claims are not so limited, nor is such language contemplated in the specification. The resultant effect of the random mutations encompassed by the claims would be highly unpredictable to one skilled in the art. It would require an undue amount of experimentation for one skilled in the art to attempt to produce the millions of possible various mutations such as insertions, deletions and substitutions of any type, amount or combination of nucleotides to produce the changes in the protein, and maintain a functional protein. For example, the mutation of any of the instant protein's amino acids, with a single substitution only, would create ($1x10^{152}$ -1) possibilities alone. As no guidance is provided regarding these possible mutational events encompassed by the claims, and given that the selection, production and screening of such a large number would constitute an undue

amount of experimentation, the breadth of the claims would not be enabled by the teachings of the specification. No working examples are presented either.

For all of these reasons, the specification is not considered to be enabling for one skilled in the art to make and use the claimed invention.

6. Claims 11-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to produce the invention commensurate in scope with these claims. The claim contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This claim contains the language, "C-terminal end of the AT2 receptor" and it would require undue experimentation on the part of the practitioner in the art to determine how much of the protein to use to practice the invention. The term reads on a protein from the C-terminal amino acid alone to the whole protein, minus the N-terminal amino acid.

The Forman factors have been outlined above. For this rejection, the amount of experimentation is not as large as above but still substantial in view of the length of the AT2 receptor. The predictability is low; it is unclear how much of a protein is needed for its function. In addition, no guidance is provided in the specification to determine how much of the protein would work as the bait protein in the assay. Furthermore, the lack of a working example is enough to tip the analysis towards nonenablement.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 2-4 and 11-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "homologous" used in Claim 2 is indefinite since, given that no percentage of homology for a homologous sequence is explicitly specified, any sequence can be considered homologous even if it has no structural relationship with the claimed nucleotide sequence. This is a term that practitioners in the art use routinely but really has no art-accepted meaning. With no definition of the degree of homology, the metes and bounds of the claims are unclear.

These claims are confusing as well. Claim 1 recites nucleic acid having one of the sequences of SEQ ID Nos. 1, 3, 5, 7 or 9. The dependent claims recite that the fragment is to be used for the detection of one of those specific sequences but the fragments of claims 2-4 red on nucleic acids having one of SEQ ID Nos. 1, 3, 5, 7 or 9 as well. Of course, the complement of one of SEQ ID Nos. 1, 3, 5, 7 or 9 could be used to detect one of those sequences but the precise sequence could not be used to detect itself. Correction of this ambiguity is required.

In claims 11-14 the term "ATIP protein" is indefinite, since the P in the abbreviation stands for protein, the term really means "AT2 interacting protein protein".

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-5 are rejected under 35 U.S.C. 102(b) as being anticipated by Bonaldo et al. and Marra et al.

Bonaldo et al. and Marra et al. teach different DNA fragments identical to SEQ ID No. 5. This clearly anticipates claim 1. The other claims are anticipated because disclosure of the sense strand of DNA constitutes an inherent disclosure of its complement as well as well as the transcripts claimed in Claim 5.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bonaldo et al. or Marra et al.

The teachings of Bonaldo et al. and Marra et al. are outlined above. It would have been obvious to one of ordinary skill in the art to place the nucleic fragments of either Bonaldo et al. or Marra et al. into an expression vector and then into a host cell in order to produce the encoded protein. Motivation would be provided by the desire to further study the protein encoded by the nucleic acids of either Bonaldo et al. or Marra et al.

Allowable Subject Matter

13. Claims 11-14 are allowable over the prior art of record. Use of host cells cotransformed with different vectors is known, see Dove et al. who teach an interaction trap assay, this is the same thing that the instant inventors have done. The other references cited teach other aspects of trap assays. However, the prior art of record fails to teach the use of any portion of the AT2 receptor in such a trap assay, nor are the specific sequences taught for this use.

Conclusion

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Wax whose telephone number is (703) 308-4471. The examiner can normally be reached on Monday - Friday, 9:00 - 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher S. F. Low can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

Robert A. Wax
Primary Examiner
Art Unit 1653